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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,431	07/27/2006	Hikaru Kai	09864/0207778-US0	4903

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EXAMINER	
BLUMEL, BENJAMIN P	
ART UNIT	**PAPER NUMBER**
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,431	KAI ET AL.	
	Examiner	Art Unit	
	BENJAMIN P. BLUMEL	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *7/27/06* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/27/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Claims 1-7 are examined on the merits.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on July 27, 2006 was filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Objections

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. The specification is objected to because pages 8, 9 and 11 contain amino acid sequences without the required specific SEQ ID NO:s.

Applicants must comply with sequence rules in order to be considered a complete response to this Office Action.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing influenza virus and Japanese Encephalitis virus in serum-free media with the ProNectin F cell binding protein, does not reasonably provide enablement for a vaccine for a virus such as Hepatitis C (from the family *Flaviviridae*) or the Hendra virus (from the family *Paramyxovirus*). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Nature of the invention/Breadth of the claims. The claimed invention is drawn to a vaccine for a virus from one of the viral families *Flaviviridae, Orthomyxoviridae, Adenoviridae, Herpesviridae, Picornaviridae, Paramyxoviridae, Togaviridae,* and *Poxviridae*. For purposes of examination, some examples of common viruses of these families are Hepatitis C, Influenza, Adenovirus type 5 (Ad5), Herpes Simplex Virus (HSV), enterovirus, Hendra virus, Venezualan Equine Encephalitis (VEE), and Vaccinia, respectively.

State of the prior art/Predictability of the art. The art does not recognize vaccines for viruses of all the claimed families. Some examples are viruses Hepatitis C, HSV and Hendra or Nipah viruses. In particular, Koff (Aliment Pharmacology and Therapy, 2007) states that while vaccines for Hepatitis A and B have been successful, a vaccine for hepatitis C has yet to be created. Koff teaches that even though a hopeful Hep C vaccine candidate did induced an antibody response, this humoral response fell short of providing a protective response. *See pages 1285, 1290 and 1291.* With regard to vaccines for HSV-1 or HSV-2, Rupp and Bernstein

(Expert Opinion of Emerging Drugs, 2008) teach that such a vaccine has yet to be developed. A leading reason is that HSV is capable of entering a latent state of infection which allows these viruses to evade a host immune system. *See pages 43 and 44.* Lastly, Halpin and Mungall teach that while ribavirin reduced mortality of patients suffering from acute Nipah viral infections, no vaccine or treat is available for vaccinating these patients. *See page 299.*

Working examples. The only working examples provided are those of producing Japanese Encephalitis virus or influenza virus in serum free media with the attachment protein ProNectin F used to attach host cells to microcarrier beads.

Guidance in the specification. The specification states that vaccines for Japanese encephalitis vaccine, a Dengue fever vaccine, a West Nile fever vaccine, an Influenza vaccine, a Rabies vaccine, a Varicella vaccine, a Polio vaccine, a Hepatitis A vaccine, a Measles vaccine, a Rubella vaccine, and a Mumps vaccine, more preferred are a Japanese encephalitis vaccine, a Dengue fever vaccine, a West Nile fever vaccine, an Influenza vaccine, a Polio vaccine, a Measles vaccine, a Rubella vaccine, and a Mumps vaccine, particularly preferred are an Influenza vaccine, a Measles vaccine, a Rubella vaccine, and a Mumps vaccine, and most preferred is an Influenza vaccine can be created.

Amount of experimentation necessary. Additional research is required in order to determine how effective a virus produced by the claimed method would be at producing a vaccine against HSV, Hendra or Hepatitis C virus.

For the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites, "...A method of producing a virus comprising: adhering adhesive cells to a support which has a polypeptide (P) having 4 to 50 cell-adhesive minimum amino acid sequences (X) per molecule…", however, it is unclear if "per molecule" is directed towards either the support, the polypeptide (P) or the target that the polypeptide (P) binds on the cell (i.e., receptor, etc.). In addition, does the limitation "…4 to 50 cell-adhesive minimum amino acid sequences…" imply that the sequences are 4 to 50 amino acids in length, or that the sequence is a minimum of 4 to 50 amino acids in length or that there is a minimum of 4 and up to 50 sequences of amino acids per molecule? Claims 2-7 are rejected since they depend from claim 1. Furthermore, given the indefinite nature the claimed invention, the following rejections are based on interpreting the claimed invention to be drawn to a protein/polypeptide on a microcarrier which binds to cells in culture, thereby immobilizing them on the microcarrier.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Kistner et al. (Developments in Biological Standardization, 1999) as evidenced by Wang and Ouyang (Bioprocess Engineering, 1999).

The claimed invention is drawn a method of producing a virus comprising: adhering adhesive cells to a microcarrier which has a polypeptide (P) having 4 to 50 cell-adhesive minimum amino acid sequences (X) per molecule, and is free from animal-origin components; culturing the adhesive cells in a medium free from animal-origin components; subculturing the cultured adhesive cells using a cell dispersing agent free from animal- origin components; and then inoculating and proliferating a virus in the cells obtained by culturing the adhesive cells. The virus produced belongs to at least one selected from a group consisting of *Flaviviridae, Orthomyxoviridae, Adenoviridae, Herpesviridae, Picornaviridae, Paramyxoviridae, Togaviridae, and Poxviridae*. The claimed invention further includes that a vaccine is produced by this method. In the present invention, "free from animal origin components" means free from components originated from homoeothermic animals, in particular, animals such as mammals (for example, human, cattle, pig, dog, rabbit, cat, and the like), birds, and fishes. *See page 4 lines 1-3 of specification).*

Kistner et al. teach producing influenza viruses in Vero cells attached to microcarriers (Cytodex-3) which contain denatured collagen (a natural cell binding protein) [as evidenced by Wang and Ouyang, page 207] with serum-free media. However, even though collagen is a protein of animal origin, the denatured form of the collagen employed by Kistner et al. is structurally distinct from that of a naturally occurring collagen molecule and therefore not of animal origin. Kistner et al. also tested the produced influenza viruses as vaccine candidates.

The produced virus was combined with alum and administered to chimpanzees. Upon challenge, all chimpanzees receiving viruses obtained form serum-free cultures where protected and also provided the highest sero-conversion as compared to viruses produced *in ovo. See pages 103, 106 and table 5.* Therefore, Kistner et al. anticipate the claimed invention.

Claims 4-6 are rejected under 35 U.S.C. 102(a) as being anticipated by Monath et al. (International Journal of Infectious Diseases, 2004).

The claimed invention is drawn to a vaccine based on at least one virus selected from a group consisting of Flaviviridae, Orthomyxoviridae, Adenoviridae, Herpesviridae, Picornaviridae, Paramyxoviridae, Togaviridae, and Poxviridae. This vaccine is produced by a method of producing a virus comprising: adhering adhesive cells to a microcarrier which has a polypeptide (P) having 4 to 50 cell-adhesive minimum amino acid sequences (X) per molecule, and is free from animal-origin components; culturing the adhesive cells in a medium free from animal-origin components; subculturing the cultured adhesive cells using a cell dispersing agent free from animal- origin components; and then inoculating and proliferating a virus in the cells obtained by culturing the adhesive cells. However, for purposes of examination, the claimed invention is interpreted as a product-by-process, which the MPEP § 2113 states that, "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." Therefore, the limitation of the process that affects that product with

regard to patentability is that of not using animal-origin components (i.e., serum-free medium [see page 5 of specification]) in the culturing of cells and virus.

Monath et al. teach the production of ACAM2000, a smallpox vaccine strain of Vaccinia, in vero cells attached to microcarriers that are cultured in serum-free media. *See page S35.* Therefore, Monath et al. anticipate the claimed invention.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers (i.e., PCT/JP05/07459 and 2004-122898 JP) have not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claims 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Kistner et al. (US Pat. 6,372,223 B1).

The claimed invention is drawn to a vaccine based on at least one virus selected from a group consisting of Flaviviridae, Orthomyxoviridae, Adenoviridae, Herpesviridae, Picornaviridae, Paramyxoviridae, Togaviridae, and Poxviridae. This vaccine is produced by a method of producing a virus comprising: adhering adhesive cells to a microcarrier which has a polypeptide (P) having 4 to 50 cell-adhesive minimum amino acid sequences (X) per molecule, and is free from animal-origin components; culturing the adhesive cells in a medium free from animal-origin components; subculturing the cultured adhesive cells using a cell dispersing agent free from animal- origin components; and then inoculating and proliferating a virus in the cells obtained by culturing the adhesive cells. However, for purposes of examination, the claimed invention is interpreted as a product-by-process, which the MPEP § 2113 states that, "Even though product-by-process claims are limited by and defined by the process, determination of

patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." Therefore, the limitation of the process that affects that product with regard to patentability is that of not using animal-origin components (i.e., serum-free medium [see page 5 of specification]) in the culturing of cells and virus.

Kistner et al. teach producing influenza virus based vaccines in Vero cells cultured in protein free media. The influenza viruses were inactivated with formalin following their harvest. Upon administering the Vero cell produced/inactivated influenza virus with alum (adjuvant), Chimpanzees presented a higher seroconversion than conventionally produced influenza viruses (i.e., *in ovo*). *See examples 1 and 3.* Therefore, Kistner et al. anticipate the claimed invention.

Summary

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN P. BLUMEL whose telephone number is (571)272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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